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1645

PATENT  
Confirmation No.: 4006

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Lily YANG, et al.      Examiner: Unassigned  
Serial No.: 10/542,117      Group Art Unit: 1645  
Filed: November 30, 2005      Docket No.: 14507-50900  
Title: **Methods of Detecting Gene Expression In Normal And Cancerous Cells**

**CERTIFICATE UNDER 37 CFR 1.8:**

I hereby certify that this correspondence is being deposited on December 5, 2006 with the United States Postal Service as first class mail, with sufficient postage, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

By: Hsiu-Ming Saunders  
Name: Hsiu-Ming Saunders

**TRANSMITTAL**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**Customer No. 24728**

Sir:

We are transmitting herewith the attached:

- Transmittal Sheet containing Certificate of Mailing (1 page)
- Supplemental Information Disclosure Statement (37 C.F.R. § 1.97(b)) (2 pages)
- Form PTO-1449 Listing Fifty-Two (52) References (3 page)
- Copies of Fifty-Two (522) Non-Patent References
- Return postcard

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Serial No.:	10/542,117	Group Art Unit:	1645
Filed:	November 30, 2005	Docket No.:	14507-50900
Title:	<b>Methods of Detecting Gene Expression In Normal And Cancerous Cells</b>		

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Alexandria, VA 22313-1450

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**SUPPLEMENTAL INFORMATION DISCLOSURE  
STATEMENT (37 C.F.R. § 1.97(b))**

Dear Sir:

With regard to the above-identified application, the items of information listed on the enclosed Form 1449 are brought to the attention of the Examiner.

In accordance with 37 C.F.R. §1.98(a)(2), a copy of each non-U.S. patent document with an abstract in English or other information listed on the enclosed Form 1449 is provided herewith, if applicable.

No representation is made that a reference is "prior art" within the meaning of 35 U.S.C. §§ 102 and 103 and Applicants reserve the right, pursuant to 37 C.F.R. § 1.131 or otherwise, to establish that the reference(s) are not "prior art." Moreover, Applicants do not represent that a reference has been thoroughly reviewed or that any relevance of any portion of a reference is intended.

Consideration of the items listed is respectfully requested. Pursuant to the provisions of M.P.E.P. 609, it is requested that the Examiner return a copy of the attached Form 1449, marked as being considered and initialed by the Examiner, to the undersigned with the next official communication.

Respectfully submitted,

MORRIS, MANNING & MARTIN, LLP

December 5, 2006

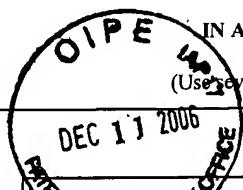
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			Applicant: Lily Yang <i>et al.</i>	Date Mailed: December 5, 2006
			Filing Date: November 30, 2005	Group Art Unit: Unassigned



U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS							
		DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION
							YES      NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)							
	1	Altieri DC and Marchisio C.; Survivin Apoptosis: An Interloper Between Cell Death And Cell Proliferation in Cancer, Lab. Invest. Vol. 79, No. 11: 1327-33, 1999.					
	2	Altieri DC; The molecular basis and potential role of survivin in cancer diagnosis and therapy, Trends in Mol. Med. Vo. 7, No. 12: 542-547, 2001.					
	3	Ambrosini G, Adida C, Altieri DC, A novel anti-apoptosis gene, survivin, expressed in cancer and lymphoma. Nature Medicine Vol. 3, No. 8: 917-21, 1997.					
	4	Anker P, Lefort F, Vasioukhin V, Lyautey J, Lederrey C, Chen XQ, Stroun M, Mulchahay HE, and Farthing MJG; K-ras Mutations Are Found in DNA Extracted From the Plasma of Patients With Colorectal Cancer. Gastroenterology; 112: 1114-1120, 1997.					
	5	Asanuma K, Moriai R, Yajima T, Yagihashi A, Yamada M, Kobayashi D and Watanab N.; Survivin as a Radioresistance Factor in Pancreatic Cancer. Jpn. J. Cancer Res. 91: 1204-1209, 2000.					
	6	Azuhata T, Scott D, Takamizawa S, Wen J, Davidoff A, Fukuzawa M and Sandler A. The Inhibitor of Apoptosis Protein Survivin Is Associated With High-Risk Behavior of Neuroblastoma. Journal of Pediatric Surgery, Vol 36, No. 12: 1785-91, 2001.					
	7	Barkin JS and Goldstein JA. Diagnostic Approach to Pancreatic Cancer. Gastroenterology Clinics Vol. 28, No. 3: 709-22, 1999.					
	8	Berrozpe G, Schaeffer J, Peinado MA, Real FX and Perucho M. Comparative Analysis of Mutations In The p53 and K-ras Genes In Pancreatic Cancer. International Journal of Cancer, 58: 185-191, 1994.					
	9	Büchler P, Conejo-Garcia JR, Lehmann G, Muller M, Emrich T, Reber HA, Büchler MW and Friess H. Real-Time Quantitative PCR of Telomerase mRNA Is Useful for the Differentiation of Benign and Malignant Pancreatic Disorders. Pancreas Vol. 22, No. 4: 331-40, 2001.					
	10	Clayton SJ, Scott FM, Walker J, Callaghan K, Haque K, Liloglou T, Xinarianos G, Shawcross S, Ceuppens P, Field JK and Fox JC. K-ras Point Mutation Detection in Lung Cancer: Comparison of Two Approaches to Somatic Mutation Detection Using ARMS Allele-specific Amplification. Clinical Chemistry 46:12: 1929-38, 2000.					
	11	Deveraux QL, Roy N, Stennicke HR, Van Arsdale T, Zhou Q, Srinivasula SM, Alnemri ES, Salvesen GS, Reed JC. IAPs block apoptotic events induced by caspase-8 and cytochrome c by direct inhibition of distinct caspases. The EMBO Journal. Vol. 17 No. 8: 2215-23, 1998.					
	12	Dubertret B, Calame M, and Libchaber A. Single-mismatch detection using gold- quenched fluorescent oligonucleotides. Nature Biotechnology Vol. 19: 365-370, 2001.					
	13	Fischer C, Büthe J, Nollau P, Hollerbach S, Schulmann K, Schmiegel W, Wagener C and Tschentscher P. Enrichment of Mutant KRAS Alleles in Pancreatic Juice by Subtractive Iterative Polymerase Chain Reaction. Laboratory Investigation Vol. 81, No. 6: 827-31, 2001.					
	14	Futakawa N, Kimura W, Yamagata S, Zhao B, Ilsoo H, Inoue T, Sata N, Kawaguchi Y, Kubota Y and Muto T. Significance of K-ras mutation and CEA level in pancreatic juice in the diagnosis of pancreatic cancer. Journal of Hepatobiliary Pancreatic Surgery Vol. 7: 63-71, 2000.					
	15	Goggins M, Hruban RH and Kern SE. BRCA2 Is Inactivated Late in the Development of Pancreatic Intraepithelial Neoplasia: Evidence and Implications. American Journal of Pathology Vol. 156, No. 5: 1767-71, 2000.					

EXAMINER	DATE CONSIDERED
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16	Gold EB, Epidemiology of and Risk Factors for Pancreatic Cancer. <i>Surg. Clin. North Am.</i> Vol. 75, No. 5: 819-843, 1995.
17	Hosch S, Braun S, and Pantel K. Characterization of Disseminated Tumor Cells. <i>Seminars in Surgical Oncology</i> , 20: 265-271, 2001.
18	Hruban RH, Sturm PD, Slebos RJ, Wilentz RE, Musler AR, Yeo CJ, Sohn TA, van Velthuysen MLF and Offerhaus GJA. Can K-ras Codon 12 Mutations Be Used to Distinguish Benign Bile Duct Proliferations from Metastases in the Liver? <i>American Journal of Pathology</i> Vol. 151, No. 4: 943-947, 1997.
19	Janocko LE, Brown KA, Smith CA, Gu LP, Pollice AA, Singh SG, Julian T, Wolmark N, Sweeney L, Silverman JF, nad Shackney SE. Distinctive Patterns of Her- 2/Neu, c-myc, and Cyclin D1 Gene Amplification by Fluorescence In Situ Hybridization in Primary Human Breast Cancers. <i>Cytometry</i> 46: 136-149, 2001.
20	Kappler M, Köhler T, Kampf C, Diestelkötter P, Würl P, Schmitz M, Bartel F, Lautenschläger C, Rieber EP, Schmidt H, Baché M, Taubert H, and Meye A. Increased Survivin Transcript Levels: An Independent Negative Predictor of Survival in Soft Tissue Sarcoma Patients. <i>International Journal of Cancer</i> 95: 360-363, 2001.
21	Kato J, Kuwabara Y, Mitani M, Shinoda N, Sato A, Toyama T, Mitsui A, Nishiwaki T, Moriyama S, Kudo J and Fujii Y. Expression of Survivin in Esophageal Cancer: Correlation with the Prognosis and Response to Chemotherapy. <i>International Journal of Cancer</i> 95: 92-95, 2001.
22	LaCasse EC, Baird S, Komeluk RG and MacKenzie AE. The inhibitors of apoptosis (IAPs) and their emerging role in cancer. <i>Oncogene</i> Vol. 17: 3247-59, 1998.
23	Li F, Ackermann EJ, Bennett CF, Rothermel AL, Plescia J, Tognin S, Villa A, Marchisio PC, and Altieri DC. Pleiotropic cell-division defects and apoptosis induced by interference with survivin function. <i>Nature cell Biology</i> Vol. 1: 461-466, 1999.
24	Li F, Ambrosini G, Chu EY, Plescia J, Tognin S, Marchisio PC and Altieri DC. Control of apoptosis and mitotic spindle checkpoint by survivin. <i>Nature</i> Vol. 396: 580-4, 1998.
25	Lüttges J, Schlehe B, Menke MA, Vogel I, Henne-Bruns D and Klöppel G. The K-ras Mutation Pattern in Pancreatic Ductal Adenocarcinoma Usually Is Identical to That in Associated Normal, Hyperplastic, and Metaplastic Ductal Epithelium. <i>American Cancer Society</i> Vol. 85: 1703-10, 1999.
26	Minamoto T, Mai M and Ronai Z. K-ras Mutation: Early Detection in Molecular Diagnosis and Risk Assessment of Colorectal, Pancreas, and Lung Cancers—A Review. <i>Cancer Detection &amp; Prevention</i> Vol. 24(1): 1-12, 2000.
27	Moore M. Urine Detection of Survivin and Diagnosis of Bladder Cancer. <i>Journal of Insurance Medicine</i> Vol. 33: 202-3, 2001.
28	Myung SJ, Kim MH, Kim YS, Kim HJ, Park ET, Yoo KS, Lim BC, Seo DW, Lee SK, Min YI and Kim JY. Telomerase activity in pure pancreatic juice for the diagnosis of pancreatic cancer may be complementary to K-ras mutation. <i>Gastrointestinal Endoscopy</i> Vol. 51, No. 6: 708-13, 2000.
29	Nakaizumi A, Uehara H, Takenaka A, Uedo N, Sakai N, Yano H, Ohigashi H, Ishikaw O, Ishiguro S, Sugano K and Tatsuta M. Diagnosis of Pancreatic Cancer by Cytology and Measurement of Oncogene and Tumor Markers in Pure Pancreatic Juice Aspirated by Endoscopy. <i>Hepato-Gastroenterology</i> 46: 31-7, 1999.
30	Nomoto S, Nakao A, Ando N, Takeda S, Kasai Y, Inoue S, Kaneko T and Takagi H. Clinical Application of K-ras Oncogene Mutations in Pancreatic Carcinoma: Detection of Micrometastases. <i>Seminars in Surgical Oncology</i> 15: 40-46, 1998.
31	Okai T, Watanabe H, Yamaguchi Y, Mouri I, Motoo Y and Sawabu N. EUS and K-ras analysis of pure pancreatic juice collected via a duodenoscope after secretin stimulation for diagnosis of pancreatic mass lesion: a prospective study. <i>Gastrointestinal Endoscopy</i> Vol. 50, No. 6: 797-803, 1999.
32	O'Shaughnessy JA, Ljung BM, Dooley WC, Chang J, Kuerer HM, Hung DT, Grant MD, Khan SA, Phillips RF, Duvall K, Euhus DM, King BL, Anderson BO, Troyan SL, Kim J, Veronesi U, Cazzaniga M. Ductal Lavage and the Clinical Management of Women at High Risk for Breast Carcinoma. <i>American Cancer Society</i> 292-8, 2002.
33	Parker SL, Tong T, Bolden S. and Wingo P., <i>Cancer Statistics</i> , 1996. <i>CA Cancer J. Clin.</i> Vol. 46: 5-27, 1996.
34	Pervin S, Singh R, and Chaudhuri G. Nitric oxide-induced cytostasis and cell cycle arrest of a human breast cancer cell line (MDA-MB-231) : Potential role of cyclin D 1. <i>Proc. of the Natl. Acad. of Sciences USA</i> , Vol. 98, No. 6: 3583-3588, 2001.
35	Poddar SK. Symmetric vs asymmetric PCR and molecular beacon probe in the detection of a target gene of adenovirus. <i>Molecular and Cellular Probes</i> 14: 25-32, 2000.
36	Poller DN, Galea M, Pearson D, Bell J, Gullick WJ, Elston CW, Blamey RW and Ellis IO. Nuclear and flow cytometric characteristics associated with overexpression of the c-erbB-2 oncprotein in breast carcinoma. <i>Breast Cancer Research &amp; Treatment</i> 20: 3-10, 1991.
37	Puig P, Urgell E, Capella G, Sancho FJ, Pujol J, Boadas J, Farré A, Lluís F, González-Sastre F, Mora J. A Highly Sensitive Method For K-ras Mutation Detection Is Useful In Diagnosis Of Gastrointestinal Cancer. <i>International Journal of Cancer</i> . 85: 73-77, 2000.

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	38	Queneau PE, Adessi GL, Thibault P, Cléau D, Heyd B, Mantion G and Carayon P. Early Detection of Pancreatic Cancer in Patients With Chronic Pancreatitis: Diagnostic Utility of a K-ras Point Mutation in the Pancreatic Juice. American Journal of Gastroenterology Vol. 96, No. 3: 700-4, 2001.
	39	Ramachandra S, Machin L, Ashley S, Monaghan P, Gusterson BA. Immunohistochemical Distribution of c-erbB-2 In <i>In Situ</i> Breast Carcinoma--A Detailed Morphological Analysis. Journal of Pathology Vol. 161: 7-14, 1990.
	40	Rozenblum E, Schutte M, Goggins M, Hahn SA, Panzer S, Zahurak M, Goodman SN, Sohn TA, Hruban RH, Yeo CJ and Kern SE. Tumor-suppressive Pathways in Pancreatic Carcinoma, Cancer Research 57: 1731-1734, 1997.
	41	Sarela AL, Macadam RCA, Farmery SM, Markham AF and Guillou PJ. Expression of the antiapoptosis gene, Survivin, predicts death from recurrent colorectal carcinoma. Gut BMJ Journals 46(5): 645-650, 2000.
	42	Satoh K, Kaneko K, Hirota M, Masamune A, Satoh A and Shimosegawa T. Expression of Survivin Is Correlated with Cancer Cell Apoptosis and Is Involved in the Development of Human Pancreatic Duct Cell Tumors. American Cancer Society, Vol. 92, No. 2: 271-278, 2001.
	43	Seki K, Suda T, Aoyagi Y, Sugawara S, Natsui M, Motoyama H, Shirai Y, Sekine T, Kawai H, Mita Y, Waguri N, Kuroiwa T, Igarashi M and Asakura H. Diagnosis of Pancreatic Adenocarcinoma by Detection of Human Telomerase Reverse Transcriptase Messenger RNA in Pancreatic Juice with Sample Qualification. Clinical Cancer Research, Vol. 7: 1976-81, 2001.
	44	Seregni E, Ferrari L, Martinetti A and Bombardieri E. Diagnostic and Prognostic Tumor Markers in the Gastrointestinal Tract. Seminars in Surgical Oncology 20: 147-166, 2001.
	45	Shibata K, Mori M, Kitano S and Akiyoshi T. Detection of ras gene mutations in peripheral blood of carcinoma patients using CD45 immunomagnetic separation and nested mutant allele specific amplification. International Journal of Oncology 12: 1333-8, 1998
	46	Sokol DL, Zhang X, Lu P and Gewirtz AM. Real time detection of DNA-RNA hybridization in living cells. Proceedings of the National Academy of Sciences of the US, Vol. 95: 11538-11543, 1998.
	47	Swana HS, Grossman D, Anthony JN, Weiss RM, Altieri DC. Tumor Content of the Antiapoptosis Molecule Survivin and Recurrence of Bladder Cancer. The New England Jounza] of Medicine, Vol. 341: 452-453, 1999.
	48	Tamm I, Wang Y, Sausville E, Scudiero DA, Vigna N, Oltersdorf T and Reed JC. IAP-Family Protein Survivin Inhibits Caspase Activity and Apoptosis Induced by Fas (CD95), Bax, Caspases, and Anticancer Drugs. Cancer Research 58: 5315-20, 1998.
	49	Tanaka K, Iwamoto S, Gon G, Nohara T, Iwamoto M and Tanigawa N. Expression of survivin and Its Relationship to Loss of Apoptosis in Breast Carcinomas. Clinical Cancer Research Vol. 6: 127-34, 2000.
	50	Yamada H, Yoshida T, Sakamoto H, Terada M and Sugimura T. Establishment Of A Human Pancreatic Adenocarcinoma Cell Line (PSN-1) With Amplifications of Both c-myc and Activated c-Ki-ras By A Point Mutation. Biochemical & Biophysical Research Communications, Vol. 140, No.1: 167-73, 1986.
	51	Z'graggen K, Centeno BA, Castillo F, Jimenez RE, Werner J and Warshaw AL. Biological implication of tumor cells in blood and bone marrow of pancreatic cancer patients, Surgery: 537-546, 2001.
	52	Tyagi S, Marras SAE, Kramer FR. Wavelength-shifting molecular beacons, Nature Biotechnology, Vol. 18: 1191-1196, 2000.

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